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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/519,008
Filing Date: December 21, 2004
Appellant(s): BELANOFF, JOSEPH K.

Mr. Kenneth A. Weber, Esq.
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed November 3, 2009 appealing from the Office action mailed December 10, 2008.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application: claims 1-4 and 8-19.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN

REJECTIONS.” New grounds of rejection (if any) are provided under the subheading “NEW GROUNDS OF REJECTION.”

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant’s brief.

(8) Evidence Relied Upon

6,150,349 Schatzberg et al. 11-2000
Ademmer et al. "Suicidal Ideation with IFN-alpha and Ribavirin in a Patient with Hepatitis C," Psychosomatics **2001**, 42:4, pp 365-367.
Dieterich, "Treatment of Hepatitis C and Anemia in Human Immunodeficiency Virus-Infected Patients," The Journal of Infectious Diseases, **2002**, 185 (Suppl 2), S128-37.
Shimizu, H. et al. "Increase in serum interleukin-6, plasma ACTH and serum cortisol levels after systemic interferon-alpha administration," Endocr. J. **1995 Aug.**, 42(4), abstract only.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

(A) Claims 1-4 and 8-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schatzberg et al. (US 6,150, 349) in view of Ademmer et al. (Suicidal Ideation with IFN- α and Ribavirin in a Patient with Hepatitis C, *Psychosomatics* **2001**, 42:4, pp 365-367).

Appellant Claims

Appellant claims a method of ameliorating the symptoms of psychosis associated with interferon-a therapy in a patient comprising administering to the patient having received interferon-a therapy and suffering from psychosis associated with the interferon- α therapy, an amount of a glucocorticoid receptor antagonist effective to ameliorate the symptoms of psychosis in the patient, with the proviso that the patient is not otherwise in need of treatment with a glucocorticoid receptor antagonist.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Schatzberg et al. teach a method of ameliorating psychosis to patient in need thereof, including the psychotic component of pathologies or conditions with psychotic symptoms (see the entire article, especially column 1 lines 19-21). The term "psychosis" can refer to a psychiatric condition or symptom associated with a medical condition, a disease state or other conditions such as a side effect of a medication or side effect of drug abuse (see the entire article, especially column 6 lines 25-32). The method of ameliorating psychosis, particularly psychosis associated with major depression, comprises administering an effective amount of a glucocorticoid receptor antagonist where the glucocorticoid receptor antagonist used in the methods can comprise a steroidal skeleton with at least one phenyl-containing moiety in the 11-beta position of the steroidal skeleton where the phenyl-containing moiety in the 11-beta position of the steroidal skeleton can be a dimethylaminophenyl moiety and the glucocorticoid receptor antagonist can comprise mifepristone (RU486), 11-13-(4- dimethyl-aminoethoxyphenyl)-I 7a-propynyl- 1713-hydroxy-4,9-estradien-3-one(RU009), and 1713-hydrox-17a -19-(4-methyl-phenyl)androst-4,9 (11)-dien-3-one (RU044) (see the entire article, especially column 3 lines 46-63; column 10 lines 7-21). The glucocorticoid antagonist can be administered by oral administration, topical administration, aerosol formulations, where the dosage of mifepristone can be about 2- 30mg per kg of body weight per day (see the entire article, especially column 20 lines 25-45; column 21 lines 56-68).

**Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)**

Schatzberg et al. do not teach ameliorating the symptoms of psychosis associated with a patient having received interferon- α therapy and is suffering from psychosis associated with interferon- α therapy by administering a glucocorticoid receptor antagonist. Schatzberg et al. do not teach administering the glucocorticoid receptor antagonist in combination with interferon- α and a second therapeutic agent. These deficiencies are cured by the teaching of Ademmer et al.

Ademmer et al. teach the state of the art treatment for hepatitis C virus (HCV) is the combination therapy with interferon alpha (IFN- α) and ribavirin (see the entire article, especially the first paragraph in the first column). One of the most serious side effects of the IFN- α treatment is the development of psychiatric symptoms; particularly depression and suicidal ideation (see the entire article, especially the first paragraph in the first column on page 365). In a case report, a 55 year old, Mr. A with a chronic active infection of HCV, started on treatment with IFN- α and ribavirin (see the entire article, especially the first paragraph under the Case Report). Immediately after starting therapy Mr. A appeared to be depressed and became progressively isolated (see the entire article, especially the second paragraph under the Case Report in column 2 on page 365). After four months of receiving treatment for his hepatitis C infection, Mr. A was admitted to a psychosomatic ward where he met criteria for major depression (see the entire article, especially the last sentence in the second paragraph under the Case Report and the third paragraph under the Case Report on page 366).

**Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)**

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to ameliorate the symptoms of psychosis associated with a patient having

received interferon- α therapy and is suffering from psychosis associated with interferon- α therapy by administering a glucocorticoid receptor antagonist and to further administer the glucocorticoid receptor antagonist in combination with interferon- α and a second therapeutic agent. One of ordinary skill in the art would have been motivated to do this Schatzberg et al. suggests the use of a glucocorticoid receptor antagonist for treating the symptoms of psychosis (e.g. major depression) caused by the side effects of a medication. Although Schatzberg et al. do not teach the specific medication for which side effects will occur, it is well known in the art that major side effects are associated with receiving IFN- α drug treatment which includes the development of psychiatric symptoms, such as major depression as taught by Ademmer et al. Thus, it would have been obvious to one of ordinary skill in the art because patients receiving IFN- α treatment are at risk for developing psychiatric symptoms and the glucocorticoid receptor antagonist is effective at treating psychosis caused by side effects of a medication. Furthermore, although Schatzberg et al. do not teach using the glucocorticoid receptor antagonist concomitantly with the interferon- α and ribavirin, it would have been obvious to one of ordinary skill in the art because it provides the patient protection against developing psychosis throughout the IFN- α treatment. Therefore, the claimed invention would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because the prior art is fairly suggestive of the claimed invention.

(B) Claims 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schatzberg et al. (US 6,150, 349) in view of Ademmer et al. (Suicidal Ideation with IFN- α and Ribavirin in a Patient with Hepatitis C, *Psychosomatics* **2001**, 42:4, pp 365-367) further in view

of Dieterich (Treatment of Hepatitis C and Anemia in Human Immunodeficiency Virus-Infected Patients, The Journal of Infectious Diseases, **2002**, 185(Suppl 2), S128-37).

Appellant Claims

Appellant claims a method of ameliorating the symptoms of psychosis associated with interferon-a therapy in a patient comprising administering to the patient having received interferon-a therapy and suffering from psychosis associated with the interferon- α therapy, an amount of a glucocorticoid receptor antagonist effective to ameliorate the symptoms of psychosis in the patient, with the proviso that the patient is not otherwise in need of treatment with a glucocorticoid receptor antagonist.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The disclosure of Schatzberg et al. is set forth above. Specifically, Schatzberg et al. teach a method of ameliorating psychosis to patient in need thereof comprising administering an effective amount of a glucocorticoid receptor antagonist. The disclosure of Ademmer et al. is set forth above. Specifically Ademmer et al. teach the state of the art treatment for hepatitis C virus (HCV) is the combination therapy with interferon alpha (IFN- α) and ribavirin. And that one of the most serious side effects of the IFN- α treatment is the development of psychiatric symptoms, particularly depression and suicide ideation.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Schatzberg et al. and Ademmer do not teach ameliorating the symptoms of psychosis associated with a patient having received interferon- α therapy and is suffering from leukemia, HIV, Human T-Cell Lymphotropic virus or cancer or has a history of substance abuse. This deficiency is cured by the teachings of Dieterich.

Dieterich teaches that co-infection of hepatitis C virus (HCV) and human immunodeficiency virus (HIV) is common, especially among intravenous drug abusers (see the entire article, especially the second paragraph under the introduction). Patients receiving IFN- α and ribavirin therapy can experience side effects such as influenza-like syndrome and other side effects that persist or increase with continued treatment such as neuropsychiatric effects including depression, anxiety, personality change etc (see the entire article, especially page \$134, the third paragraph in the first column and the second and third paragraph in the second column)

**Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)**

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to ameliorate the symptoms of psychosis associated with a patient having received interferon- α therapy and is suffering HIV and has a history of substance abuse comprising administering a glucocorticoid receptor antagonist. One of ordinary skill in the art would have been motivated to do this because Dieterich suggest that it is common for a patient to be co-infected with HCV and HIV, especially among intravenous drug users. It is also known that co-infected patients treated with interferon- α and ribavirin can develop neuropsychiatric effects such as depression. Thus, it would have been obvious to one of ordinary skill in the art to treat a co-infected patient who has a history of substance abuse receiving IFN- α treatment with a

glucocorticoid receptor antagonist because are they are still prone to developing side caused by side effects of the medication (i.e. IFN- α treatment). Therefore, the claimed invention would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made because the prior art is fairly suggestive of the claimed invention.

(10) Response to Argument

(A) Appellant traverses the rejection in section 9(A) above by arguing that the Office's position is improper, because allegedly (i) it is based on an unreasonable interpretation of the claims, (ii) it ignores claim limitations, (iii) it is circular, (iv) in Appellant's opinion it is irrelevant to issue of obviousness, and (v) the Office is relying on improper hindsight reasoning. More succinctly, Appellant concedes that the Office has established a prima facie case of obviousness, but urges that the teachings of the art as a whole, especially with reference to the Gisslinger reference that Appellant cited, tips the scale of evidence towards unobviousness.

The Office respectfully disagrees with Appellant's traversal arguments. Regarding (i), Appellant argues that the previous Examiner has incorrectly interpreted the time frame for administration of a glucocorticoid receptor antagonist (GRA) to ameliorate the symptoms of psychosis associated with interferon-alpha therapy. The Office finds this argument unpersuasive. The previous Examiner was correct to note that the claimed method does not recite any particular time from for the administration of the GRA to ameliorate psychosis. Furthermore, as Schatzberg clearly articulates multiple times, psychosis in patients is recognized as being due to glucocorticoid dysfunction (e.g. col. 1, lines 51-53) that may be detected, for example, by changes in cortisol levels (col. 2, lines 21-22) and can be treated by administration

of a GRA, such as mifepristone (col. 2, lines 53-55; col. 3, lines 45-52; col. 9, lines 34-40; claims 1-13, etc.). Schatzberg also explicitly teaches the amelioration of psychosis by the administration of a GRA (e.g. claim 13 and col. 7, lines 49-53). Moreover, Ademmer et al establishes that it was well known the psychosis, such as suicidal ideation, is a well-recognized symptom of IFN-alpha therapy. The fact that psychosis as a side effect does not occur in all patients receiving IFN-alpha therapy is irrelevant. It is sufficient that the art recognizes that IFN-alpha can induce psychosis and that when psychosis is detected that psychosis can be ameliorated by administration of a GRA.

Regarding (ii), Appellant urges that the previous examiner ignored the proviso language in the rejected claims (i.e. "...with the proviso that the patient is not otherwise in need of treatment with a GRA). This is unpersuasive, because Schatzberg explicitly indicates that the administration of a GRA is suitable for ameliorating the mental disorder or syndrome of psychosis (col. 7, lines 48-53), wherein "ameliorating" is explicitly defined at column 4, lines 45-51 of Schatzberg to mean, "any indicia of success in the treatment of a pathology or condition...or an improvement in a patient's physical or mental well-being." Thus, contrary to Appellant's argument Schatzberg's teachings are not limited to the treatment of psychotic major depression.

Regarding (iii) and (iv), Appellant's characterization of the previous arguments of record is not persuasive, because these reflect Appellant's biased opinion. Furthermore, Appellant attempts to distract attention from the key facts of the rejection by his discussion of "irrelevant truths," but this discussion does not change the ultimate conclusion that the claimed method remains obvious per the teachings of the prior art. The facts are that the prior art of record

establishes that glucocorticoid dysfunction is a recognized etiology of psychosis, GRA administration is suitable to treat and ameliorate psychosis, and IFN-alpha administration is well-known in the art to have as one of its adverse effects suicidal ideation (i.e. psychosis). Thus, for the ordinary skilled artisan to arrive at the claimed invention requires no leap of faith or quantum leap in thinking to connect the dots and conclude that treatment of psychosis associated with IFN-alpha is obvious and would have had a reasonable expectation of success, because psychosis is art-recognized as resulting from glucocorticoid regulation dysfunction, IFN-alpha is known to induce psychosis, and GRAs are indicated for the treatment of psychosis.

Regarding (v), in response to Appellant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Appellant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As explained above, the conclusion of obviousness is not based on hindsight, but the explicit teachings of the art recording the etiology of psychosis (Schatzberg), the recognized fact that IFN-alpha therapy may induce psychosis (Ademmer), and that GRA administration is indicated for the amelioration of psychosis (Schatzberg). The rejection is maintained for the aforementioned reasons.

(B) Appellant does not separately traverse rejection 9(B). Therefore, the Office's rebuttal of Appellant's traversal arguments to the rejection restated in section 9(A) above is herein

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incorporated by reference. Additionally, it is noted that Dieterich's teachings further support the notion that the prior art recognized the connection between IFN-alpha therapy and psychosis. The rejection is maintained for the reasons articulated above.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616

Conferees:

/James H Alstrum-Acevedo/
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